

In the Claims

1. (Previously Presented) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) formulation for oral administration, said formulation comprising particles, the cores of which comprise an SSRI which is fluvoxamine or a pharmaceutically-acceptable salt thereof, said core having thereon a rate-controlling membrane coating which allows controlled release of said SSRI over a period of not less than about 12 hours following oral administration.
2. (Original) A formulation according to Claim 1, wherein the particles are pellets.
3. (Cancelled)
4. (Currently Amended) A formulation according to Claim 1 2, wherein the rate-controlling membrane coating comprises a mixture of a major proportion of a pharmaceutically acceptable film-forming, water-insoluble polymer and a minor proportion of a pharmaceutically acceptable film-forming, water-soluble polymer in a selected ratio, the selected ratio of said water-insoluble polymer to said water-soluble polymer being effective to permit a SSRI release rate which allows controlled release of said SSRI over a period of not less than about 12 hours following oral administration.
5. (Currently Amended) A formulation according to Claim 1 4, wherein the rate-controlling membrane coating contains an ammonio methacrylate co-polymer.

Claims 6 to 19 (Cancelled)

20. (Previously Presented) A formulation according to Claim 1, wherein the core further comprises an organic acid, the SSRI component and the organic acid being present in a ratio of from 50:1 to 1:50.

21. (Cancelled)

22. (Cancelled)

23. (Currently Amended) A formulation according to Claim 1, wherein said membrane coating comprises an ammonio methacrylate copolymer and a plasticizer, the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating being in an amount of from about 4% to about 15% of the weight of the cores present in said formulation, is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate from the particles exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 15% of the total SSRI is released after 0.5 of an hour of measurement in said apparatus;
- (b) no more than about 25% of the total SSRI is released after 1 hour of measurement in said apparatus;

- (c) between about 20% and about 75% of the total SSRI is released after 2 hours of measurement in said apparatus;
- (d) not less than about 75% of the total SSRI is released after 4 hours of measurement in said apparatus; and
- (e) not less than about 85% of the total SSRI is released after 6 hours of measurement in said apparatus.

24. (Currently Amended) A formulation according to Claim 1, wherein said membrane coating comprises an ammonio methacrylate copolymer and a plasticizer, the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating being in an amount of from about 4% to about 15% of the weight of the cores present in said formulaton, is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a laquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate from the particles exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 20% of the total SSRI is released after 4 hours of measurement in said apparatus;
- (b) no more than about 45% of the total SSRI is released after 6 hours of measurement in said apparatus;

- (c) between about 45% and 80% of the total SSRI is released after 8 hours of measurement in said apparatus;
- (d) not less than about 70% of the total SSRI is released after 10 hours of measurement in said apparatus; and
- (e) not less than about 80% of the total SSRI is released after 12 hours of measurement in said apparatus.

25. (Previously Presented) A formulation according to Claim 1 in a form suitable for oral administration.

26. (Previously Presented) A formulation according to Claim 1 in a form suitable for oral administration and comprising a blend of said particles in admixture with an immediate release form of SSRI or a pharmaceutically acceptable salt thereof to ensure a rapid attainment of effective therapeutic blood levels.

27. (Previously Presented) A formulation according to Claim 26, wherein the immediate release form of SSRI comprises pellets.

28. (Currently Amended) A formulation according to Claim 25, wherein said membrane coating comprises an ammonio methacrylate copolymer and a plasticizer, the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating being in an amount of from about 4% to about 15% of the weight of the cores present in said formulation, is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15%

~~of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate when measured *in vitro* using a USP type II dissolution apparatus (paddle) according to US Pharmacopoeia XXII in 0.05 M phosphate buffer at pH 6.8 substantially corresponds to the following dissolution pattern:~~

- (a) no more than 20% of the total SSRI is released after 1 hour of measurement in said apparatus;
- (b) no more than 60% of the total SSRI is released after 2 hours of measurement in said apparatus;
- (c) not less than 20% of the total SSRI is released after 4 hours of measurement in said apparatus;
- (d) not less than 35% of the total SSRI is released after 6 hours of measurement in said apparatus;
- (e) not less than 50% of the total SSRI is released after 8 hours of measurement in said apparatus;
- (f) not less than 70% of the total SSRI is released after 10 hours of measurement in said apparatus; and
- (g) not less than 75% of the total SSRI is released after 12 hours of measurement in said apparatus.

29. (Currently Amended) A formulation according to Claim 25, wherein

said membrane coating comprises an ammonio methacrylate copolymer and a plasticizer, the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating being in an amount of from about 4% to about 15% of the weight of the cores present in said formulation, is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate from the particles exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

- (a) no more than about 20% of the total SSRI is released after 1 hour of measurement in said apparatus;
- (b) no more than about 45% of the total SSRI is released after 2 hours of measurement in said apparatus;
- (c) between about 20% and about 70% of the total SSRI is released after 4 hours of measurement in said apparatus;
- (d) between about 35% and about 85% of the total SSRI is released after 6 hours of measurement in said apparatus;
- (e) not less than about 50% of the total SSRI is released after 8 hours of measurement in said apparatus.
- (f) not less than about 70% of the total SSRI is released after 10

hours of measurement in said apparatus; and

(g) not less than about 75% of the total SSRI is released after 12 hours of measurement in said apparatus.

30. (Currently Amended) A formulation according to Claim 1, wherein said membrane coating comprises an ammonio methacrylate copolymer and a plasticizer, the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating being in an amount of from about 4% to about 15% of the weight of the cores present in said formulation, is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein the SSRI release rate from the particles exhibits the following *in vitro* dissolution pattern when measured using a USP type II dissolution apparatus (paddle) according to US Pharmacopeia XXII in 0.05 M phosphate buffer at pH 6.8:

(a) no more than about 50% of the total SSRI is released after 2 hours of measurement in said apparatus;

(b) not less than about 35% of the total SSRI is released after 6 hours of measurement in said apparatus; and

(c) not less than about 80% of the total SSRI is released after 22 hours of measurement in said apparatus.

31. (Previously Presented) A formulation according to Claim 4, wherein the

core further comprises an organic acid, the SSRI component and the organic acid being present in a ratio of from 50:1 to 1:50.

32. (Previously Presented) A formulation according to Claim 5, wherein the core further comprises an organic acid, the SSRI component and the organic acid being present in a ratio of from 50:1 to 1:50.

33. (Previously presented) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate controlled release SSRI formulation according to Claim 1.

34. (Currently Amended) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate controlled release SSRI formulation according to Claim 24 25.

35. (Cancelled)

36. (Previously Presented) The formulation according to Claim 1, wherein said rate controlling polymer is SSRI-permeable.

37. (Previously Presented) The formulation according to Claim 1, wherein said rate controlling polymer is SSRI-permeable and water soluable.

38. (Previously Presented) The formulation according to Claim 1, wherein said rate controlling polymer is SSRI-permeable and water insoluable.

39. (Previously Presented) The formulation according to Claim 25, wherein said formulation is in capsule form.
40. (Previously Presented) The formulation according to Claim 25, wherein said formulation is in tablet form.

Claims 41 to 44 (Cancelled)

45. (Previously Presented) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate controlled release SSRI formulation according to Claim 24.
46. (Previously Presented) The formulation according to Claim 24, wherein said formulation is in tablet form.
47. (Previously Presented) A multiparticulate controlled release selective serotonin reuptake inhibitor (SSRI) formulation for oral administration, which comprises particles, the core of which comprises an SSRI which is fluvoxamine or a pharmaceutically-acceptable salt thereof, said core coated with a rate-controlling polymeric acrylate or methacrylate lacquer substance which allows controlled release of said SSRI over a period of not less than about 12 hours following oral administration.
48. (Previously Presented) A formulation according to Claim 47 wherein said substance is said acrylate lacquer.

49. (Previously Presented) A formulation according to Claim 47 wherein said substance is said methacrylate lacquer.
50. (Previously Presented) A formulation according to Claim 47 wherein said substance is a lacquer which contains a mixture of said acrylate and methacrylate.
51. (Previously Presented) A formulation according to Claim 47 wherein said substance is an acrylic resin comprising a copolymer of acrylic and methacrylic acid esters having a low content of quaternary ammonium groups.

Claims 52 to 54 (Cancelled)

55. (Currently Amended) The formulation of Claim 1 wherein said membrane coating comprises an ammonio methacrylate copolymer and a plasticizer, the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating being in an amount of from about 4% to about 15% of the weight of the cores present in said formulation is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer and wherein.
56. (Currently Amended) The formulation of Claim 55 wherein the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the cores present in said formulation said weight gain is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of

~~the weight of the core.~~

57. (Previously Presented) A method for the treatment of depression or obsessive compulsive disorder treatable with an SSRI, comprising administering to a patient suffering from one of said conditions a therapeutically effective amount of a multiparticulate controlled release SSRI formulation according to Claim 55.
58. (Currently Amended) The formulation of Claim 55 wherein the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating is in an amount of about 8% of the weight of the cores present in said formulation ~~said weight gain is in an amount of about 8% of the weight of the core.~~
59. (Currently Amended) A unit dose formulation which is effective in supplying fluvoxamine to the blood of a patient such that, following a single application of the unit dose to the patient, the amount of circulating fluvoxamine ( $AUC_{0-\infty}$ ) in the blood serum of the patient is about 128 ~~275~~ to about 1,900 ng/ml.h, said formulation comprising particles, the cores of which comprise an SSRI which is fluvoxamine or a pharmaceutically-acceptable salt thereof, said core having thereon a rate-controlling membrane coating which allows controlled release of said SSRI over a period of not less than about 12 hours following oral administration.
60. (Currently Amended) The formulation of Claim 59 ~~58~~ wherein said membrane coating comprises an ammonio methacrylate copolymer and a plasticizer, the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating being in an

amount of from about 4% to about 15% of the weight of the cores present in said formulation is present in an amount such that it contributes to the particle a weight gain of from about 4% to about 15% of the weight of the core and is formed from a lacquer substance comprising ammonio methacrylate copolymer.

61. (Currently Amended) The formulation of Claim 60 wherein the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the cores present in said formulation said weight gain is in an amount of 4%, 6%, 8%, 10%, 12%, or 15% of the weight of the core.
62. (Currently Amended) The formulation of Claim 58 wherein said amount of circulating fluvoxamine ( $AUC_{0-\infty}$ ) in the blood serum of the patient is about 128 275 to about 1,175 ng/ml.h.
63. (Currently Amended) The formulation of Claim 60 wherein the combined amount of said ammonio methacrylate copolymer and said plasticizer in said membrane coating is in an amount of about 8% of the weight of the cores present in said formulation said weight gain is in an amount of about 8% of the weight of the core.
64. (New) A formulation according to Claim 1 wherein said particles are beads.
65. (New) A formulation according to Claim 64, wherein said rate-controlling membrane coating comprises a pharmaceutically-acceptable film-forming, water-insoluble polymer in an amount effective to obtain

controlled release of an SSRI over a period of not less than about 12 hours following oral administration.

66. (New) A formulation according to Claim 65 wherein said rate-controlling membrane comprises further a plasticizer.